

Mosunetuzumab (Mosun) monotherapy for elderly/unfit patients (pts) with first-line diffuse large B-cell lymphoma (DLBCL) continues to show promising safety and efficacy with durable complete responses

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Summary

Ongoing Phase I/II study evaluating the safety and efficacy of mosunetuzumab monotherapy in elderly and/or unfit pts with previously untreated DLBCL.

48 pts had received treatment at data cut-off.

Median age was 83 years (range: 65–100).

Mosunetuzumab monotherapy had a favourable toxicity profile in older and/or unfit pts with previously untreated DLBCL.

The most common adverse event (AE) was cytokine release syndrome (CRS) (29.2% of pts).

Overall response rate (ORR) 61.5% in efficacy-evaluable pts.

No Gr ≥3 CRS events were reported.

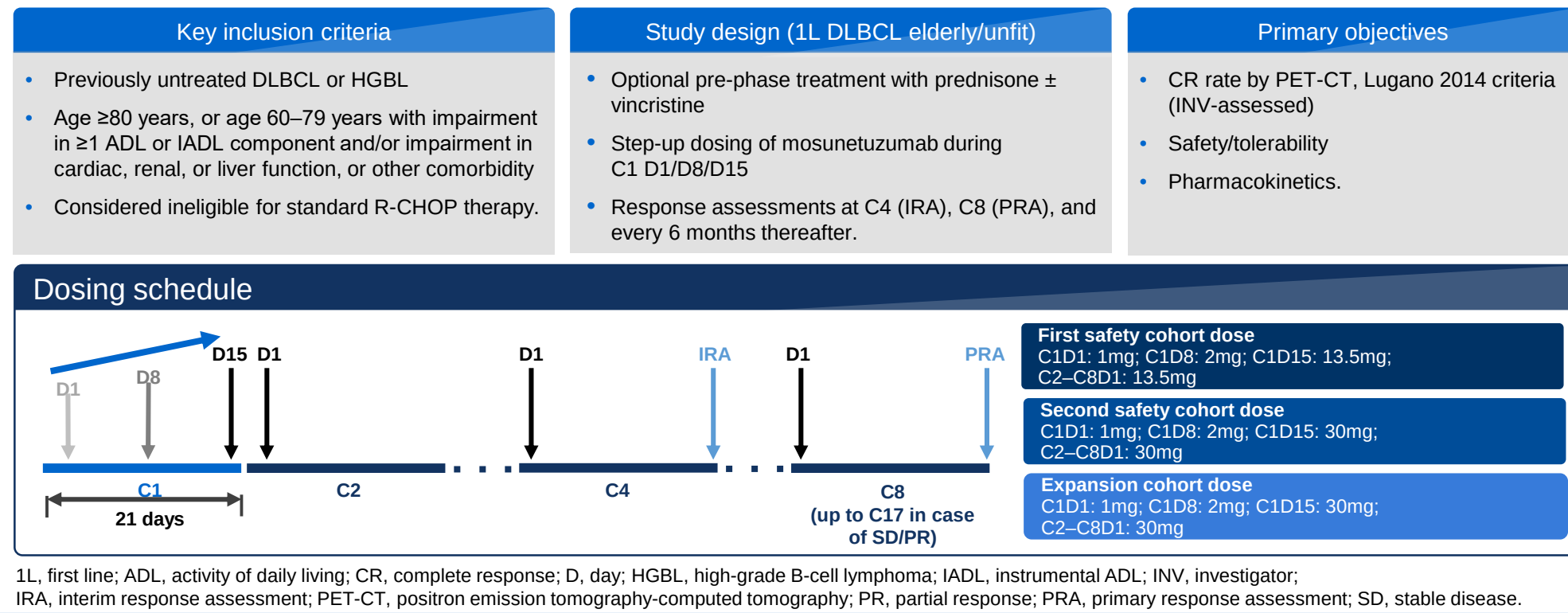
Background

- Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is standard of care for pts with previously untreated DLBCL, but it may be unsuitable for some older and/or unfit pts.^{1,2}
- Real-world data suggest that most elderly pts (aged ≥80 years) with previously untreated DLBCL do not receive R-CHOP at the standard dose, and that the attenuated R-CHOP or other R-based regimens often given are associated with inferior outcomes.³ Better tolerated and more efficacious treatments are needed for these pts.
- Mosunetuzumab is a CD20×CD3 bispecific antibody that has manageable toxicity and promising efficacy in pts with relapsed/refractory DLBCL.⁴
- An ongoing, multicentre, Phase I/II study (NCT03677154) is evaluating the safety and efficacy of mosunetuzumab monotherapy in elderly and/or unfit pts with previously untreated DLBCL considered unsuitable for standard R-CHOP therapy.⁵

NCT03677154: Ongoing Phase I/II study evaluating the safety and efficacy of mosunetuzumab monotherapy in elderly and/or unfit pts with previously untreated DLBCL

- Pts received mosunetuzumab monotherapy per the dosing schedule outlined in **Figure 1**.

Figure 1. Study design



At data cut-off (12 April 2021), 48 pts had received mosunetuzumab monotherapy

- Eight pts were enrolled into the 13.5mg safety cohort, seven into the 30mg safety cohort and 33 into the 30mg expansion cohort.
- The median number of mosunetuzumab cycles received was 7 (range: 0–16).

Most pts were aged ≥80 years, and all pts had an ECOG performance status score ≤2

- Of 12 pts aged <80 years, 5 had impaired renal function, 2 had impaired cardiac function with or without impairment in ≥1 ADL and/or IADL, and 5 had impairment in ≥1 ADL and/or IADL only.
- 21 pts received pre-phase treatment with prednisone ± vincristine.

Table 1. Baseline pt and disease characteristics

n (%) unless stated	1L DLBCL (N=48)
Median age, years (range)	83 (65–100)
Aged ≥80 years	36 (75.0)
Aged <80 years	12 (25.0)
Female	31 (64.6)
IPI score ≥2	37 (77.1)
ECOG performance status	
0	9 (18.8)
1	23 (47.9)
2	16 (33.3)
Ann Arbor Stage	
I	7 (14.6)
II	15 (31.3)
III	6 (12.5)
IV	20 (41.7)
Elevated LDH	23 (47.9)
Cell of origin	
GCB	20 (41.7)
Non-GCB*	23 (47.9)
WHO subtype	
DLBCL	39 (81.3)
DHL/THL	9 (18.8)

*Locally assessed by immunohistochemistry.
DHL, double-hit lymphoma; ECOG, Eastern Cooperative Oncology Group; GCB, germinal centre B-cell; IPI, International Prognostic Index; LDH, lactate dehydrogenase; THL, triple-hit lymphoma; WHO, World Health Organization.

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Mosunetuzumab monotherapy had a manageable safety profile in older pts

- Most pts (72.9%) had ≥1 AE that was considered treatment-related by investigators.
- The most common AEs were CRS (29.2% of pts), fatigue (18.8%), and abdominal pain (14.6%; **Table 2**). Febrile neutropenia (Gr 3) was observed in one pt only.
- The most frequently reported Gr 3 or Gr 4 AE was neutropenia (10.4% of pts).
- One pt discontinued treatment due to AEs (renal failure and disease progression).
- One Gr 5 (fatal) AE was observed (sudden death, due to natural causes per investigator assessment).

Table 2. AE summary

n (%)	1L DLBCL (N=48)
AEs with incidence ≥10% by PT	45 (93.8)
CRS	14 (29.2)
Fatigue	9 (18.8)
Abdominal pain	7 (14.6)
Chills	5 (10.4)
Rash maculo-papular	5 (10.4)
Neutropenia	5 (10.4)
Decreased appetite	5 (10.4)
Gr 3–4 AEs with incidence ≥5% by PT	17 (35.4)
Neutropenia	5 (10.4)
Serious AEs	17 (35.4)
Gr 5 (fatal) AEs	1 (2.1)
AEs leading to discontinuation	1 (2.1)

PT, preferred term.

CRS events* were Gr 1 or Gr 2 and occurred during the first cycle of mosunetuzumab only

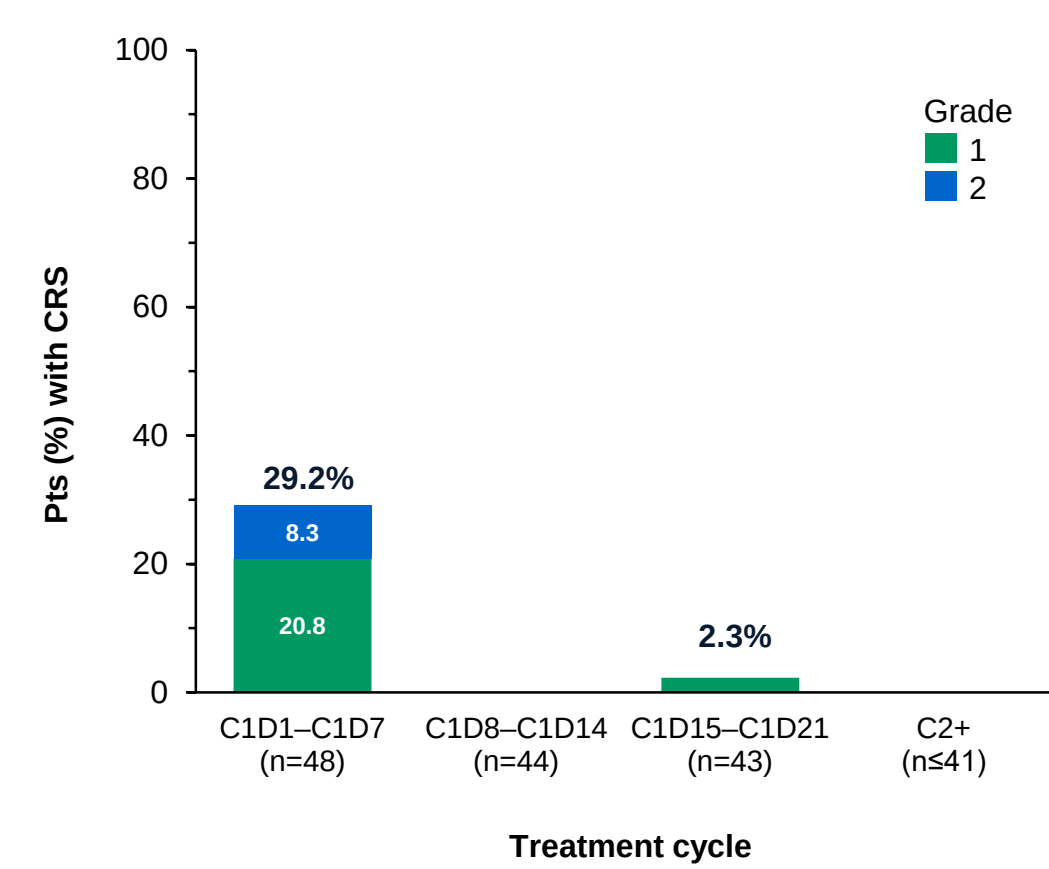
- The most frequent CRS symptoms were pyrexia (11/14 pts, 78.6%) and chills (6/14 pts, 42.9%).
- All CRS events occurred during C1 and were Gr 1 or Gr 2 (**Figure 2**).
- Gr 2 CRS events (4/14 pts) were treated with supportive care in all pts and steroids in one patient. No pressors or tocilizumab were used, and no treatment in the intensive care unit was required.

Table 3. CRS* summary

n (%) unless stated	1L DLBCL (N=48)
Any CRS	14 (29.2)
Gr 1 CRS	10 (20.8)
Gr 2 CRS	4 (8.3)
Gr ≥3 CRS	0
Use of tocilizumab for CRS, n (%)	0
Median time to onset, days (range)	1 (1–2)
Median duration, days (range)	1 (1–2)

*As defined by Lee et al. 2019 criteria.⁶

Figure 2. CRS* by cycle and grade



Mosunetuzumab monotherapy was efficacious in older and/or unfit pts

- Median duration of follow-up was 9.4 months (range: 0.2–22.7), although follow-up for some pts in the expansion cohort was very limited.
- ORRs and CR rates in efficacy-evaluable pts were 61.5% (24/39) and 43.6% (17/39), respectively (**Table 3**).
- Eight of 17 complete responders had a follow-up of ≥12 months and maintained a complete remission (**Figure 3**).

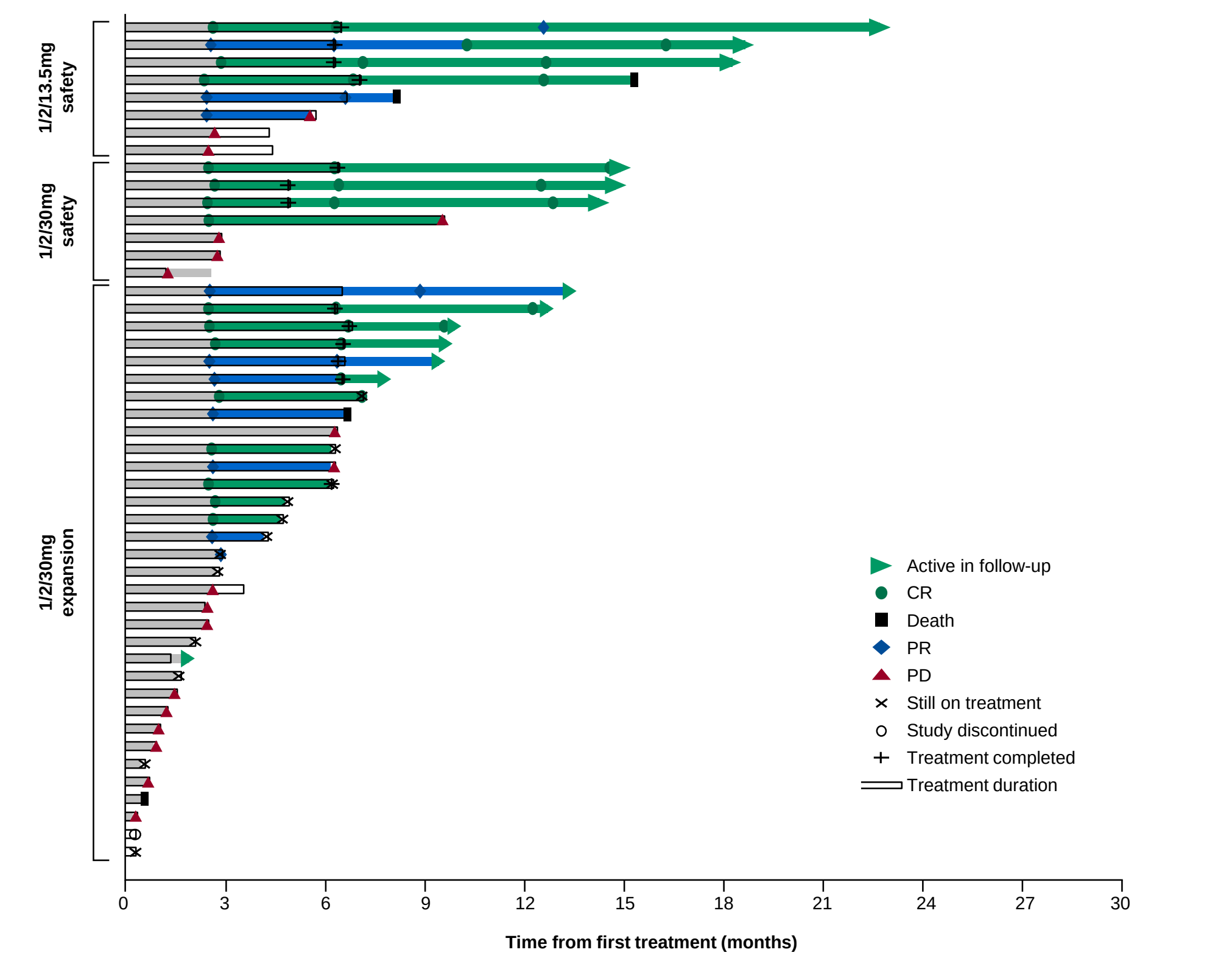
Table 3. Best overall response by investigator in efficacy-evaluable pts*

n (%)	ORR	CR	PR	SD	PD
All patients (n=39)	24 (61.5)	17 (43.6)	7 (17.9)	1 (2.6)	9 (23.1)
13.5mg cohort (n=8)	6 (75.0)	4 (50.0)	2 (25.0)	0	2 (25.0)
30mg cohort (n=31)	18 (58.1)	13 (41.9)	5 (16.1)	1 (3.2)	7 (22.6)

*Assessed by PET-CT after 4 or 8 cycles using Lugano 2014 criteria.

PD, progressive disease.

Figure 3. Duration of response

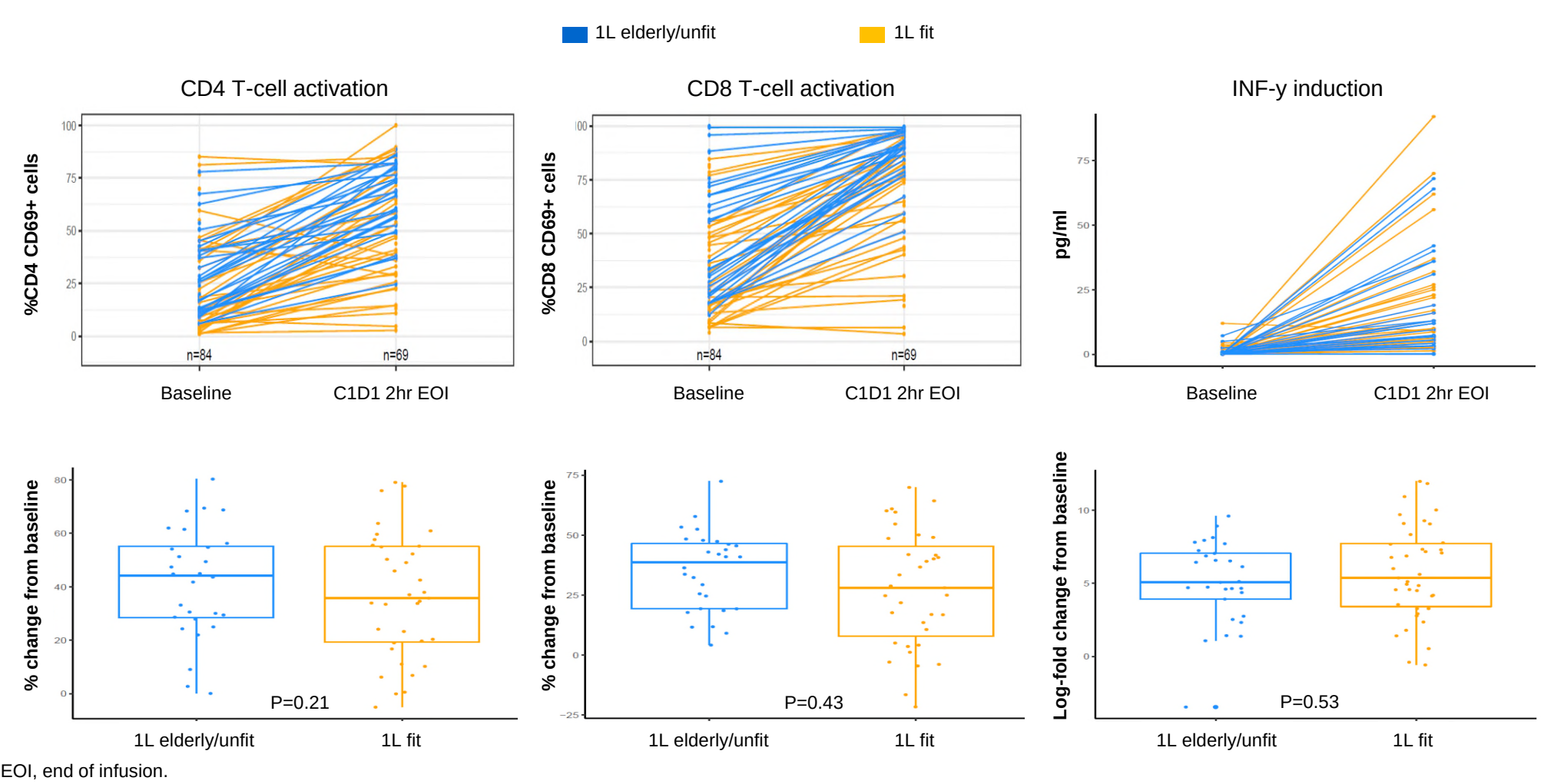


*Assessed with or without PET-CT.

Pharmacodynamic changes in peripheral blood

- Pharmacodynamic changes in peripheral blood in C1, including T-cell activation and cytokine production, were similar between elderly/unfit pts with previously untreated DLBCL who received mosunetuzumab monotherapy in the current study and fit pts with previously untreated DLBCL who received mosunetuzumab-CHOP in an ongoing Phase Ib/II study (NCT03677141)⁷ (**Figure 4**).

Figure 4. Pharmacodynamic changes in peripheral blood



Conclusions

Mosunetuzumab monotherapy has a favorable toxicity profile in older and/or unfit pts with previously untreated DLBCL. CRS events were Gr 1 or Gr 2 and were limited to C1.

Mosunetuzumab continues to show promising efficacy as monotherapy in previously untreated elderly/unfit pts, with durable CRs observed.

These data suggest a potential future role for mosunetuzumab, as monotherapy or in chemotherapy-free or chemotherapy-light combinations, in older and/or unfit pts with previously untreated DLBCL who are considered unsuitable for standard R-CHOP therapy.

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